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How epigenetics affects twins

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The largest twin study on epigenetic profiles yet reveals the extent to which lifestyle and age can impact gene expression, an international research team reports in this week's *PNAS*. Senior author Manel Esteller of the Spanish National Cancer Center in Madrid and colleagues found that 35% of twin pairs had significant differences in DNA methylation and histone modification profiles.

"These findings help show how environmental factors can change one's gene expression and susceptibility to disease, by affecting epigenetics," Esteller told *The Scientist*.

Esteller and colleagues in Sweden, Denmark, Spain, England, and the United States studied 80 sets of identical twins, ranging in age from 3 to 74 years. Their aim was to explore what role epigenetics plays in generating phenotypic differences between genetically identical twins.

The researchers analyzed the twins' global DNA methylation and histone H3 and H4 acetylation in samples from lymphocytes, buccal mucosal epithelial cells, skeletal muscle biopsies, and subcutaneous fat. They quizzed participants on their health, nutritional habits, physical activities, drug treatments, and consumption of tobacco, alcohol, and drugs. They also checked their height and weight.

Statistical analysis suggested that older twin pairs were more epigenetically different than younger twins. It also revealed that twins who reported having spent less time together during their lives, or who had different medical histories, had the greatest epigenetic differences. Gene expression microarray analysis revealed that in the two twin pairs most epigenetically distinct from each other–the 3- and 50-year-olds–there were four times as many differentially expressed genes in the older pair than in the younger pair, confirming that the epigenetic differences the researchers saw in twins could lead to increased phenotypic differences.

Arturas Petronis of the University of Toronto, who did not participate in this study, called the research "excellent" in "quantifying how genetically identical individuals could differ in gene expression on a global level due to epigenetics. It is good to have data that confirms what we long suspected."

Future twin studies can focus on disease-specific epigenetic effects, Petronis said. "There are thousands of cases when there are no good explanations for different susceptibilities to complex diseases in individuals with the same genetic background and, in most cases, similar environments. If we shift our emphasis to epigenetic factors, we can now come up with some interesting putative mechanisms that would explain such phenotypic differences," Petronis told *The Scientist*. "Maybe some loci are very dynamic epigenetically, while others are stable."

Randy Jirtle of Duke University Medical Center, who did not participate in this study, suggested investigating how aging- or lifestyle-related epigenetic changes affect imprinted genes, which are normally expressed in a parent-of-origin dependent manner. "For instance, IGF2 is usually only expressed from the father's copy. People with biallelic expression of IGF2 are more susceptible to colon cancer, and likely breast cancer and prostate cancer," he told *The Scientist*. "So epigenetic changes due to old age or other factors could lead to overexpression or underexpression of imprinted genes."

George Martin of the University of Washington in Seattle, who was not involved in this research, cautioned that future studies needed to look at purified cell types using techniques such as flow cytometric separation. "As you grow older, you have shifts in your proportions of cell types—for instance, more memory T cells and less naive T cells. And you can expect each type to have different gene expression profiles. So when you work with a mixed tissue sample, you can't be sure whether a shift in enzyme activity is due to a shift in gene expression or simply a shift in the proportions of different cell types in the sample," he told *The Scientist*.

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